community. A prompt reporting of suspected and diagnosed cases of malaria has permitted immediate interviews, the identification of the area of residence and of exposure, and a prompt assessment of malaria risk to others. Swift action and early diagnosis have reduced the spread of malaria. During 1989 and 1990, no second wave of cases occurred following an initial recognition of malaria transmission. In addition, early diagnosis has reduced the need for hospital admission among those who were infected.

The occurrence of malaria in San Diego and California is not unique. In 1990, local transmission of malaria was recognized in Florida,[3] another area where *Anopheles* species mosquitoes are endemic and free-standing water is available. The pattern of malaria transmission in San Diego County reminds us that the elements necessary to sustain the spread of this and other "manageable" health problems are present. The challenge to medical practitioners is to take a complete history and identify all possible exposures. Laboratories are challenged in examining for parasites and other organisms rarely seen in local residents. Consultation may be obtained from local county and state health departments.

The containment of parasites or bacteria requires maintaining sanitation, personal hygiene, and adequate housing. These outbreaks of malaria remind us that we are at risk for the spread of the disease. Only the maintenance of a sanitary, safe environment and preventive activities can eliminate the effects of this illness in the community.

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Daunorubicin, Amsacrine, and Sinus Arrest

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CARDIAC RHYTHM and conduction disturbances have been associated with the use of both the anthracycline antibiotics doxorubicin (Adriamycin) and daunorubicin and the aminoacridine amsacrine. They have been noted with routine clinical use in humans and under experimental conditions in animals. These disturbances have consisted of atrial fibrillation and atrial flutter, sinus bradycardia and sinus tachycardia, ventricular premature contractions, and ventricular tachycardia, in addition to the loss of voltage on the surface electrocardiogram (ECG), the appearance of fascicular blocks, and nonspecific and ischemic changes in the ST segment. First- and second-degree heart block have been reported clinically with the use of doxorubicin but not with that of amsacrine.[1,2] Atrioventricular dissociation has been described in at least three cases involving the use of daunorubicin.[3,4] While these rhythm disturbances are usually asymptomatic, there have been reports of sudden death temporally associated with the administration of either class of agents and thought to have been caused by ventricular tachycardia or ventricular fibrillation.[2,5,6] Sinus arrest has not been described with either class of agent. We report the case of a patient with acute myelogenous leukemia in whom the administration of these agents was temporally associated with the appearance of sinus arrest accompanied by a junctional escape rhythm. Furthermore, amsacrine therapy was also associated with brief episodes of ventricular asystole.

(Kindman LA, Almenoff JS, Narurkar VA, Blake K: Daunorubicin, amsacrine, and sinus arrest. West J Med 1991 Apr; 154:466-467)

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Report of a Case

The patient, a 42-year-old Vietnamese man, was diagnosed with acute myelogenous leukemia in May 1987.* He presented with constitutional symptoms, leukemia cutis, and a leukocyte count of 203 × 10^9 per liter. Before this, he was in excellent health, having a history of borderline hypertension controlled by diet alone but no other cardiac risk factors. Remission was successfully induced with a regimen of daunorubicin hydrochloride, 60 mg per m^2; cytarabine (formerly cytosine arabinoside), 18 grams per m^2; and 6-thioguanine, 18 mg per m^2. Four months later, he was readmitted with a relapse of his disease in the skin, sclerae, and meninges. A routine admission ECG revealed normal sinus rhythm, a rate of 84 per minute with a PR interval of 0.16 seconds, a QRS duration of 0.04 seconds, and a corrected QT interval of 0.41 seconds. The QRS axis was 4 degrees, and there was a nonspecific T wave abnormality in lead F. Salvage chemotherapy consisting of etoposide (VP-16-123), 100 mg per m^2 daily for five days, and cytarabine, 3 grams per m^2 daily for five days, was administered. In addition, intrathecal methotrexate therapy was initiated. The treatment was well tolerated, aside from persistent nausea managed with the intravenous administration of the antiemetics droperidol, 1 to 2 mg every six hours; diphenhydramine hydrochloride, 25 to 50 mg every four to six hours; lorazepam, 1 to 2 mg every six hours; and metoclopramide hydrochloride, 50 mg every six hours. Concomitant therapy included the antibiotics mezlocillin, gentamicin sulfate, and cefazolin sodium for the empiric treatment of fever while he was neutropenic. Because of a poor response to therapy, daunorubicin, 55 mg per m^2, was given over two hours following premedication with the above antiemetics. Daily infusions of both cytarabine and etoposide were continued. Six hours after completion of the daunorubicin infusion, the patient's blood pressure was 80/50 mm of mercury and the heart rate 50 beats per minute, both decreased from their baseline values of 110/70 mm of mercury and 90 to 110, respectively.

An ECG showed sinus arrest with a junctional escape rate of 50 and retrograde atrial activity. Occasional sinus com-

*Stanley Schrier assisted in the care of this patient and provided helpful comments.

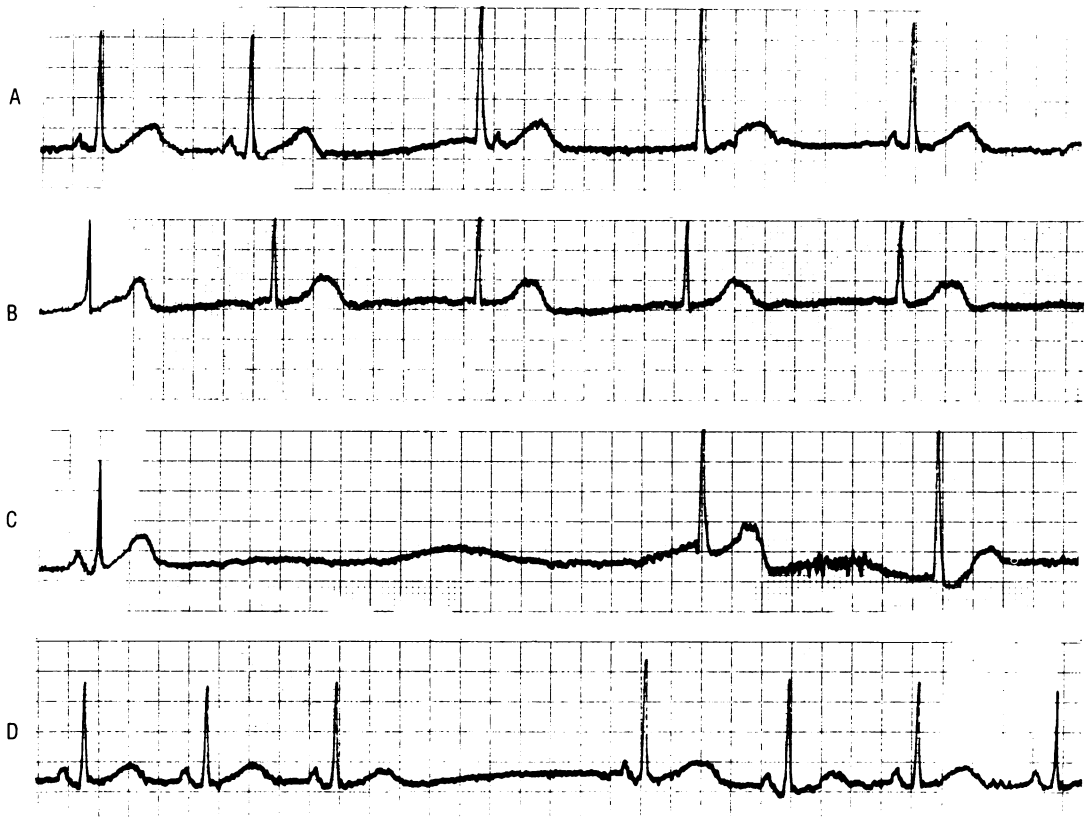

Figure 1.—Representative electrocardiographic tracings show the abnormalities described in the text: **A,** Sinus arrest followed an infusion of daunorubicin hydrochloride. **B,** Junctional rhythm followed the first dose of amsacrine. **C** and **D** are continuous. Sinus arrest and ventricular asystole followed the second dose of amsacrine.

plexes were observed (Figure 1-A). There was no response to the administration of atropine sulfate, 2 mg. At this time, the patient's serum calcium, potassium, and magnesium levels were 2.12 mmol per liter (8.5 mg per dl), 4.4 mmol per liter, and 1.4 mmol per liter, respectively. An echocardiogram showed normal ventricular contractility and borderline left atrial enlargement. The patient was placed on continuous cardiac monitoring with a transcutaneous pacing system at the bedside. Twelve hours after sinus rhythm was restored, amsacrine, 125 mg per m^2, was substituted for daunorubicin and was infused over two hours. Two hours after completion of the infusion, several brief episodes of junctional rhythm were noted on the monitor (Figure 1-B). The patient remained asymptomatic, with a blood pressure of 110/60 mm of mercury. No further arrhythmias were noted for the next 20 hours. A second dose of amsacrine, 125 mg per m^2, was administered. An hour later, sinus arrest with a junctional escape rhythm rate of 50 per minute was noted on the monitor, accompanied by several brief episodes of ventricular asystole, of which the longest was four seconds in duration (Figure 1-C and -D). By six hours, sinus rhythm had returned, and no further episodes of sinus arrest or asystole were noted. At this time, serum potassium and calcium values were 4.5 mmol per liter and 2.05 mmol per liter (8.2 mg per dl), respectively.

The patient continued to receive the aforementioned antibiotic and antiemetic therapy for the next five days, without cardiovascular side effects. Further anthracycline or aminoacridine therapy was withheld because of the poor clinical response. Remission was not achieved, and the patient died of septic complications two weeks later. During this follow-up period, no further episodes of sinus arrest or ventricular asystole were noted. Sinus tachycardia as rapid as 140 beats per minute and considered appropriate to his clinical state was noted. Permission for an autopsy was not granted.

Comment

Amsacrine is known to be cardiotoxic, but its use is generally thought to be associated with fewer cardiovascular side effects than that of the anthracyclines. While various atrial arrhythmias have been attributed to the toxic effects of both classes of drug, this is the first reported instance of sinus arrest. This case shows that both types of agents may cause sinus node dysfunction. In addition, ventricular asystole accompanied the sinus arrest that followed the amsacrine infusion. Sudden death in patients undergoing antineoplastic therapy with anthracyclines and with amsacrine has been ascribed to the occurrence of ventricular tachycardia. These observations suggest that asystole may be an additional mechanism of sudden death in patients undergoing treatment with these agents.

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